

# OCT Anatomic & Temporal Biomarkers in Uveitic Macular Edema

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# Financial Disclosures

- DG: EyePoint (C), Allergan (C), Genentech (C)
- BK: Commercial Relationship(s);Clearside Biomedical, Inc.:Code E (Employment);Clearside Biomedical, Inc.:Code I (Personal Financial Interest)
- TC: Commercial Relationship(s);Clearside Biomedical, Inc.:Code E (Employment);Clearside Biomedical, Inc.:Code I (Personal Financial Interest)

# Background

- In clinical practice, physicians often base treatment decisions on both BCVA and OCT assessment.
- There is limited information on longitudinal structure-functional correlations in Uveitic Macular Edema (UME).
- This study assessed these relationships, focusing on baseline anatomic features with potential prognostic value for visual response.

# Methods

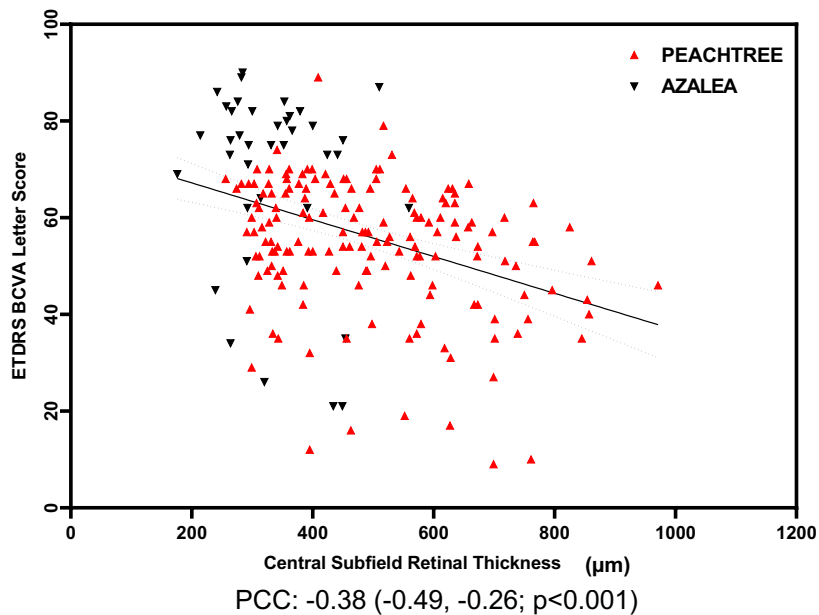
- Post hoc analysis of 198 eyes with NIU enrolled in two phase 3, 24 week clinical trials with CLS-TA<sup>1, 2</sup>.
- Assessed relationships between BCVA and
  - Ellipsoid zone (EZ) integrity
  - Presence and location of cystoid spaces
  - Presence and location of subretinal fluid (SRF)
- Correlation analyses were performed to describe the relationship at baseline, and between change from baseline.
- A longitudinal treatment-response analysis modeled the temporal relationship between change in BCVA and CST.

**NIU: noninfectious uveitis; CLS-TA: investigational formulation of triamcinolone acetonide for suprachoroidal injection**

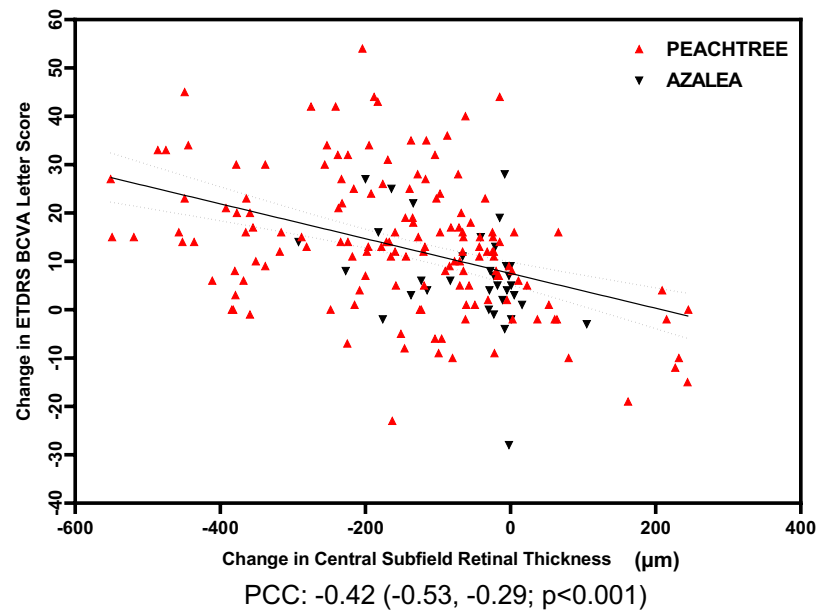
1. Yeh S, Khurana RN, Shah M, et al. Efficacy and Safety of Suprachoroidal CLS-TA for Macular Edema Secondary to Noninfectious Uveitis: Phase 3 Randomized Trial. *Ophthalmology*. 2020;127(7):948-955. doi:10.1016/j.ophtha.2020.01.006  
2. Henry CR, Shah M, Barakat MR, et al. Suprachoroidal CLS-TA for non-infectious uveitis: an open-label, safety trial (AZALEA) [published online ahead of print, 2021 Feb 5]. *Br J Ophthalmol*. 2021;bjophthalmol-2020-318019. doi:10.1136/bjophthalmol-2020-318019

# Moderate Relationships Between BCVA and CST

## Baseline



## Change from Baseline at Week 24

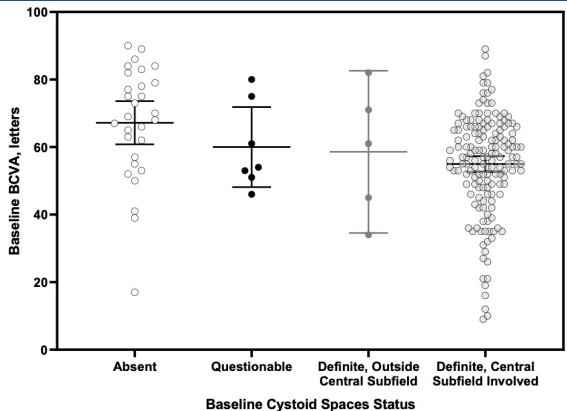
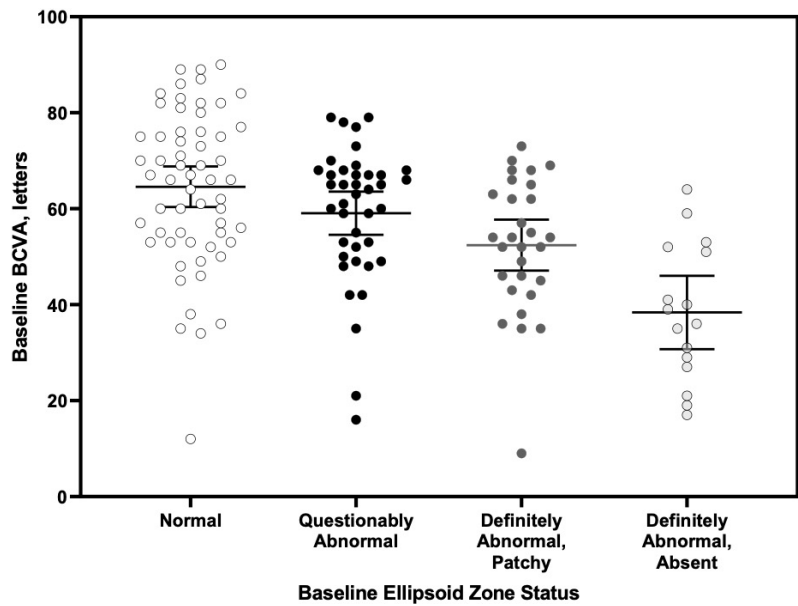


PCC: Pearson Correlation Coefficient and 95% Confidence Interval

Ciulla TA, Kapik B, Grewal DS, Ip MS. Visual Acuity in Retinal Vein Occlusion-, Diabetic-, and Uveitic Macular Edema: Central Subfield Thickness and Ellipsoid Zone Analysis [published online ahead of print, 2020 Oct 29]. *Ophthalmol Retina*. 2020;S2468-6530(20)30429-2. doi:10.1016/j.oret.2020.10.016

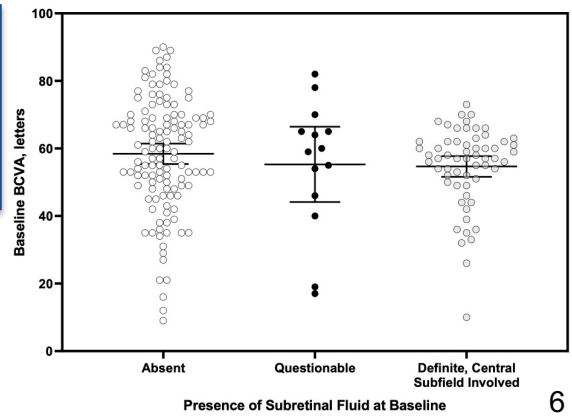
# Relationship between Baseline BCVA and EZ Status, Cystoid Spaces, SRF at Baseline

**Baseline BCVA v. Baseline EZ:**  
 Mean BCVA *statistically significantly* worsened with each EZ grade ( $p \leq 0.050$ )



**Baseline BCVA v. Baseline Cystoid Spaces:**  
 Differences between grades and BCVA not statistically significant

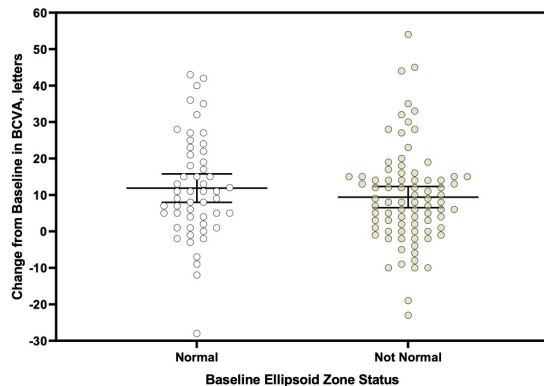
**Baseline BCVA v. Baseline SRF:**  
 Differences between grades and BCVA not statistically significant



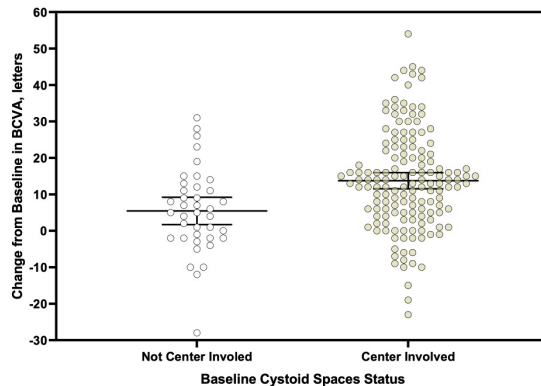
All pair-wise comparisons to 'Definitely abnormal (absent)' group were statistically significant ( $p \leq 0.034$ ) after adjustment for multiple comparisons. **Horizontal lines represent the sample mean and 95% confidence interval.**

# Relationship between Change in BCVA and EZ Status, Cystoid Spaces, SRF at Baseline

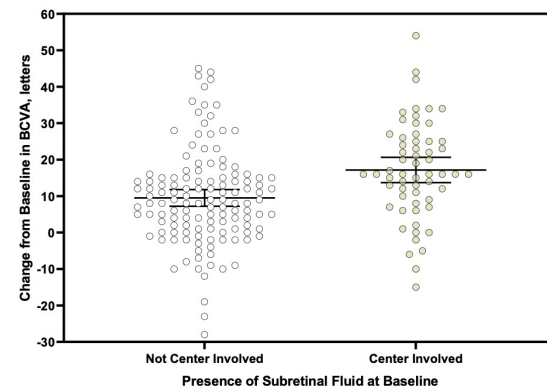
## Change in BCVA (Week 24) v. Baseline EZ Status



## Change in BCVA (Week 24) v. Baseline Cystoid Spaces Status



## Change in BCVA (Week 24) v. Baseline SRF Status



Eyes with normal EZ at baseline experienced a **greater improvement in BCVA** versus eyes with EZ considered not normal.

11.9 letters vs. 9.4 letters,  $P=0.006$

Eyes without center involved (CI) cystoid spaces at baseline showed **less improvement at 24 weeks** versus eyes with CI.

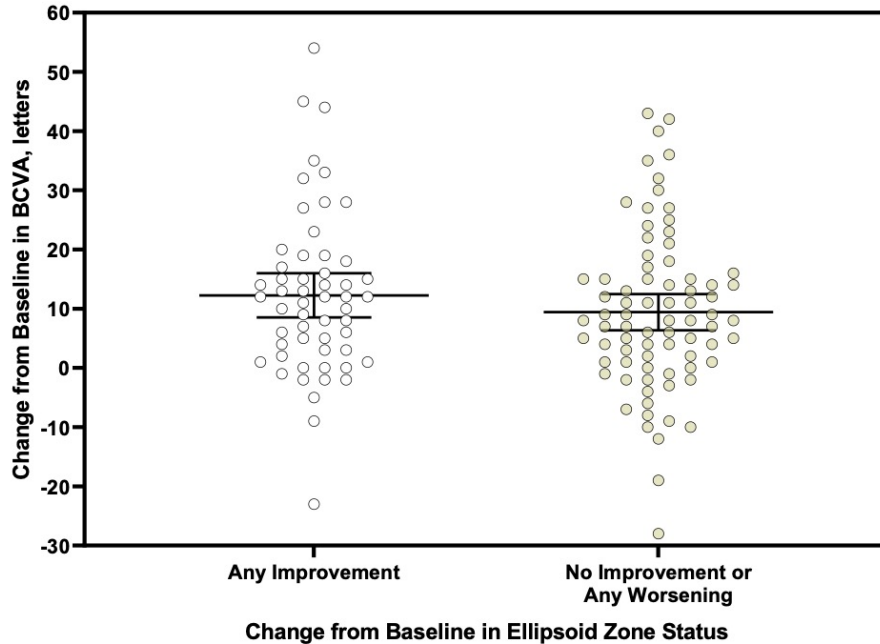
5.5 letters vs 13.7 letters;  $P = 0.012$

Eyes without CI SRF at baseline showed **less improvement at 24 weeks** versus eyes with CI

9.5 letters vs 17.2 letters;  
 $P < 0.001$

# Relationship between Change in BCVA and Change in EZ Status

## Change in BCVA v. Change in EZ at Week 24



Eyes showing any improvement in EZ status at week 24 experienced a mean change from baseline in BCVA that was numerically greater, versus eyes that did not show any change from baseline or who worsened.

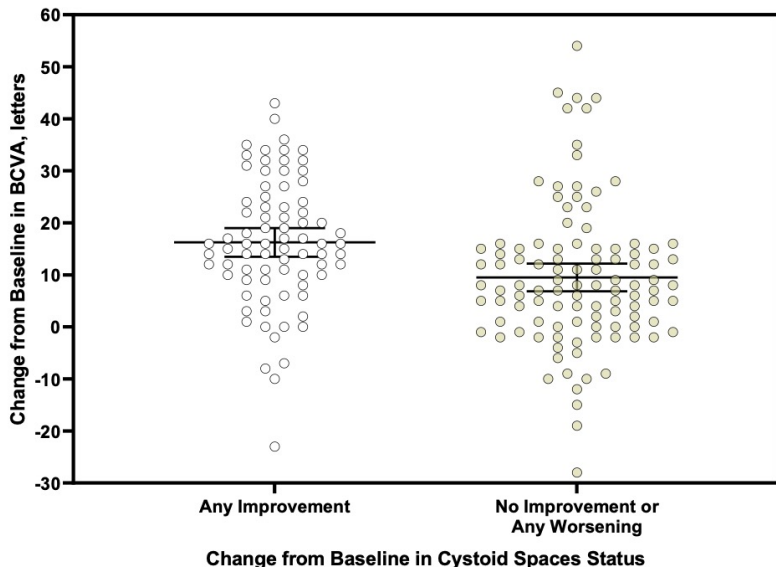
Not statistically significant  
(11.4 letters vs. 10.0 letters;  $P=0.512$ )

*Horizontal lines represent the sample mean and 95% confidence interval. P-value based on an ANCOVA model with baseline EZ status as the independent variable and baseline CST, baseline BCVA, and age as covariates.*

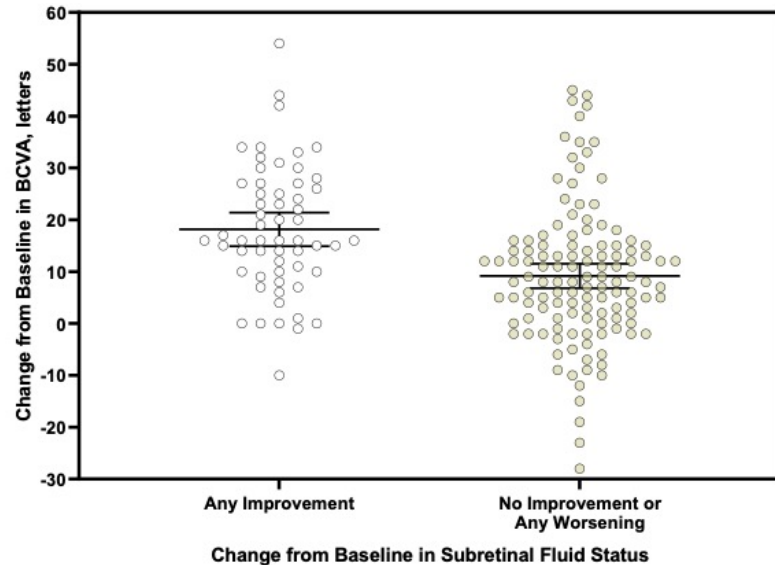


# Relationship between Change in BCVA and Change in Cystoid Space & SRF Status

## Change in BCVA v. Change in Cystoid Spaces at Week 24



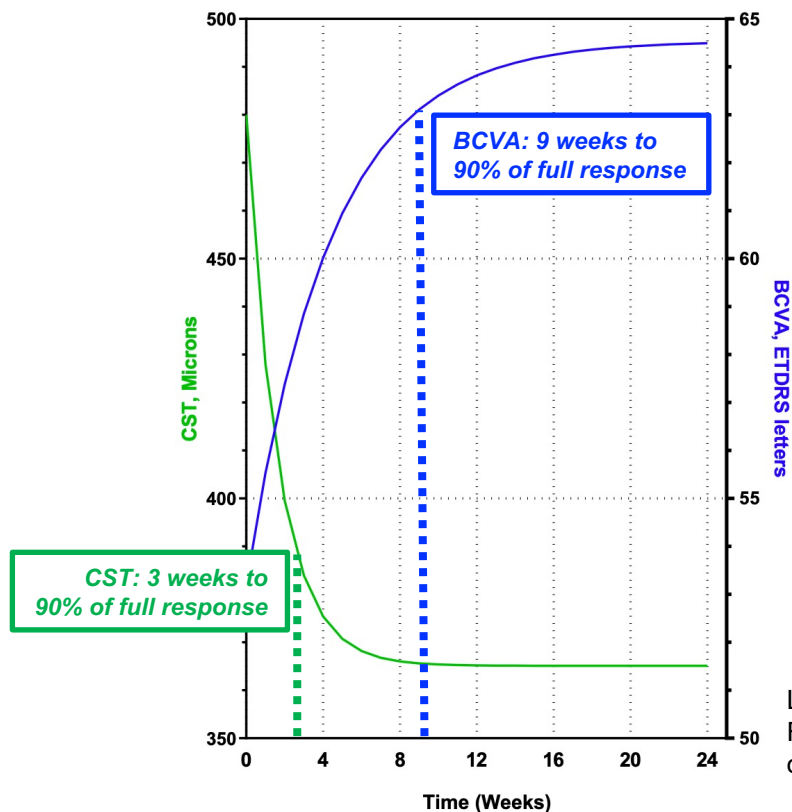
## Change in BCVA v. Change SRF at Week 24



Eyes that showed any improvement in cystoid spaces and/or SRF showed a significantly greater improvement in BCVA ( $P < 0.001$  for both)

# Longitudinal modeling showed more rapid response for CST

## Typical BCVA and CST Response from CLS-TA



Longitudinal modeling showed that the **frame of response was more rapid for CST than BCVA.**

- **CST required approximately 3 weeks** to reach over 90% of full response
- **BCVA required approximately 9 weeks** to reach the same magnitude of response.

Longitudinal non-linear mixed effects model based on methods according to the US FDA guidance for determining population pharmacokinetics and the EU guidance on reporting population pharmacokinetic analysis results.

# Conclusion

- In NIU, normal EZ, central cystoid spaces, or SRF at baseline predict improved therapeutic response.
- Eyes with early anatomic response demonstrated better BCVA response at 24 weeks
- Anatomic response may precede visual response in UME by one month or more.